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Preliminary Amendment
U.S. Application No. 10/692,856

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

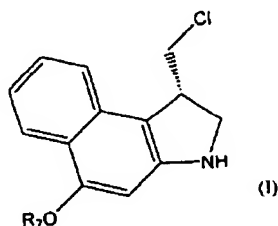
1. (original): A prodrug comprising an analog of CC-1065 in which the phenolic group of the alkylating portion of the molecule is protected and wherein said prodrug further comprises a linker capable of conjugating said prodrug to a cell binding agent.
2. (original): The prodrug of claim 1 wherein said linker comprises a thiol or a disulfide bond.
3. (original) The prodrug of claim 1 wherein said protecting group increases water-solubility of said drug,
4. (original) The prodrug of claim 3 wherein said protecting group is selected from the group consisting of a piperazino carbamate, a 4-piperidino-piperidino carbamate and a phosphate.
5. (original): The prodrug of claim 1 wherein said linker comprises a polyethylene glycol of the formula $-(O(CH_2)_2)_n-$, wherein n is an integer from 2 to 1000.
6. (original): A composition comprising the prodrug of claim 1 and a pharmaceutically acceptable carrier.
7. (original): A prodrug comprising an analog of a *seco*-cyclopropabenzindole-containing cytotoxic drug selected from the group consisting of analogs formed from a first subunit of formula (I) covalently linked to a second subunit of the formula (II), (III), (IV), (V),

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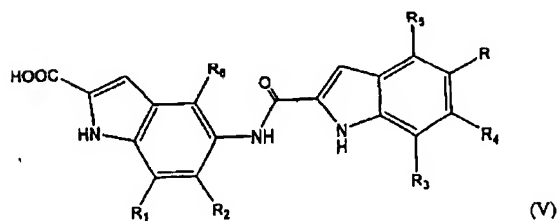
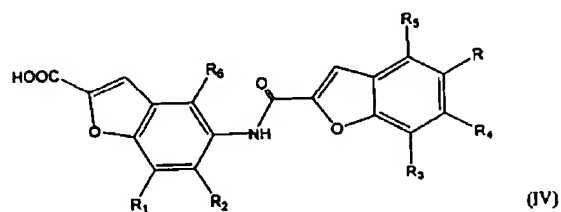
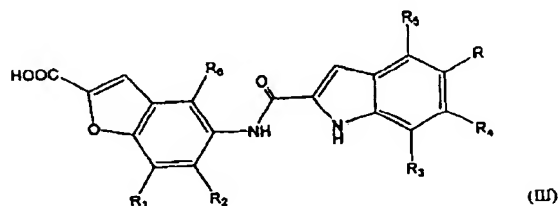
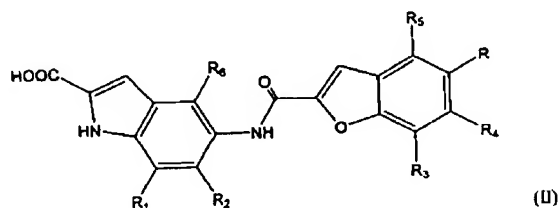
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(VI), (VII), (VIII) or (IX) via an amide bond from the secondary amino group of the pyrrole moiety of the first subunit to the C-2 carboxyl of the second subunit,

wherein the formula (I) is as follows:

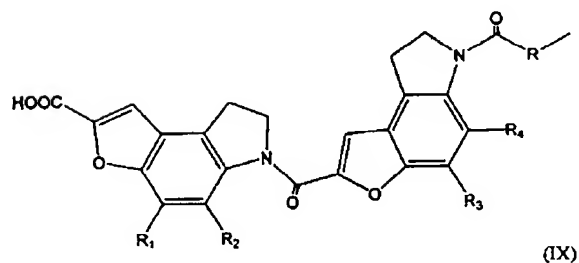
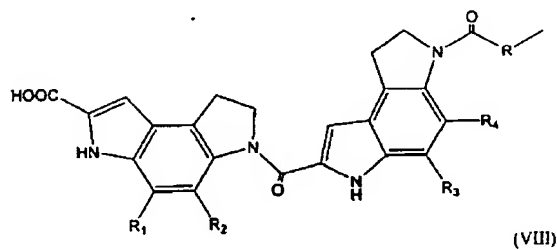
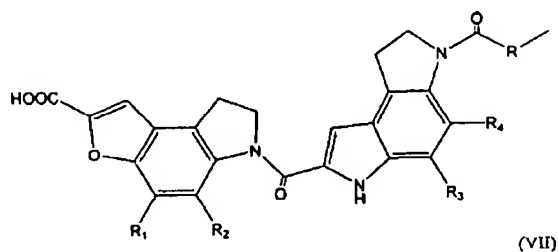
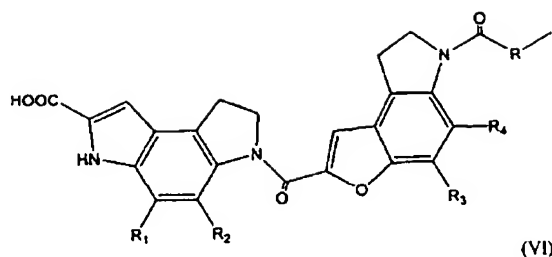


wherein the formulae (II)-(IX) are as follows:



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wherein R represents a moiety that enables linkage of said prodrug to a cell binding agent;
wherein R₁-R₆ are each independently hydrogen, C₁-C₃ linear alkyl, methoxy, hydroxyl, primary amino, secondary amino, tertiary amino, or amido;
and wherein R₇ is an enzyme-cleavable protecting group.

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8. **(original):** The prodrug of claim 7, wherein R comprises a thiol or a disulfide bond.
9. **(original):** The prodrug of claim 7, wherein R₁-R₆ are hydrogen.
10. **(original):** The prodrug of claim 7, wherein R₇ is selected from the group consisting of a piperazino carbamate, a 4-piperidino-piperidino carbamate and a phosphate.
11. **(original):** The prodrug of claim 10, wherein R represents a moiety that enables linkage of the prodrug to a cell binding agent via a disulfide bond.
12. **(currently amended):** The prodrug of claim 10, wherein said second subunit is represented by formula (II), (III), (IV), (V), (VI), (VII), (VIII) or (IX) and wherein R₁-R₆ are hydrogen.
13. **(original):** The prodrug of claim 12 which is (S)-N-[2-((1-chloromethyl)-1,2-dihydro-5-[(4-methylpiperazino)carbonyloxy]-3H-benz(e)indol-3-yl)carbonyl]-1H-indol-5-yl]-5-[(3-methyldithio-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.
14. **(original):** The prodrug of claim 12 which is (S)-N-[2-((1-chloromethyl)-1,2-dihydro-5-[(4-methylpiperazino)carbonyloxy]-3H-benz(e)indol-3-yl)carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.
15. **(original):** The prodrug of claim 12 which is (S)-N-[2-((1-chloromethyl)-1,2-dihydro-5-[(4-piperidino-piperidino)carbonyloxy]-3H-benz(e)indol-3-yl)carbonyl]-1H-indol-5-yl]-5-[(3-methyldithio-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

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16. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-[(4-piperidino-piperidino)carbonyloxy]-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

17. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-(phosphonoxy)-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-methyldithio-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

18. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-(phosphonoxy)-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

19. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-(dibenzylphosphonoxy)-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-methyldithio-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

20. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro-1H-indole-2-carboxamide, or a salt or an isomer thereof.

21. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-methyldithio-1-oxopropyl)-amino]-1H-indole-2-carboxamide, or a salt or an isomer thereof.

22. (original): The prodrug of claim 12 which is (S)-N-[2-[(1-chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz(e)indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(15''-methyldithio-

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4'',7'',10'',13''- tetraoxapentadecyl -1-oxopropyl)-amino]-1*H*-indole-2-carboxamide, or a salt or an isomer thereof.

23. **(original):** A prodrug conjugate comprising a cell binding agent linked to one or more of the prodrugs of claim 1 or claim 7.

24. **(original):** The prodrug conjugate of claim 23 wherein said cell binding agent is an antibody or a fragment thereof.

25. **(original):** A composition comprising the prodrug of claim 7 and a pharmaceutically acceptable carrier.

26. **(original):** A method for treating a subject, comprising administering to a subject in need thereof an effective amount of the composition of claim 6 or 25.

27. **(original):** A method for treating a subject, comprising administering to a subject in need thereof an effective amount of the prodrug conjugate of claim 24.

28. **(original):** The prodrug of claim 7 wherein said linker comprises polyethylene glycol of the formula $-(O(CH_2)_2)_n-$, wherein n is an integer from 2 to 1000.